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NEWS	3	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	4	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	5	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	6	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	7	MAR 02	GBFULL: New full-text patent database on STN
NEWS	8	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	9	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	10	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	11	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	12	MAR 22	PATDPASPC - New patent database available
NEWS	13	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	14	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	15	APR 04	EMBASE - Database reloaded and enhanced

NEWS EXPRESS	JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
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=> s trichothecene
L1          5456 TRICHOTHECENE

=> s l1 and (gastric motility)
L2             0 L1 AND (GASTRIC MOTILITY)

=> s l1 and (obesity or diet? or overeat? or satia? or (food intake))
L3           478 L1 AND (OBESITY OR DIET? OR OVEREAT? OR SATIA? OR (FOOD INTAKE))

=> s l3 and (DOn or (4 deoxynivalenol))
L4            66 L3 AND (DON OR (4 DEOXYNIVALENOL))

=> s l4 and P2x1 and (non desensitiz?) and agonist#
L5             0 L4 AND P2X1 AND (NON DESENSITIZ?) AND AGONIST#

=> s l4 and (P2x1 receptor)
L6             0 L4 AND (P2X1 RECEPTOR)

=> s l6 and oral?
L7             0 L6 AND ORAL?

=> s l5 and oral?
L8             0 L5 AND ORAL?

=> s l4 and oral?
L9            20 L4 AND ORAL?

=> d l9 1-20 ibib abs

L9   ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2003:999884  CAPLUS
```

DOCUMENT NUMBER: 140:235011
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil
AUTHOR(S): Moon, Yuseok; Pestka, James J.
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI, 48824-1224, USA
SOURCE: Journal of Nutritional Biochemistry (2003), 14(12), 717-726
CODEN: JNBIEL; ISSN: 0955-2863
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperelevation and mesangial IgA deposition in mice that can mimic early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) may play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) can suppress **DON**-induced IgAN, we hypothesized that FO may inhibit the induction of IL-6 expression by **DON** in vivo and in vitro. Mice were fed modified AIN 93G **diet** with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 wk and then exposed acutely to **DON** by **oral** gavage. **DON**-induced blood plasma IL-6 and splenic mRNA elevation in FO-fed mice were suppressed after 8 wk compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was suppressed in the spleen of mice fed FO, whereas p38 was not. Splenic COX-2 mRNA expression, which enhances the **DON**-induced IL-6, was also decreased by FO, whereas blood plasma levels of the COX-2 metabolite PGE2 were not affected. To confirm the in vivo findings, the effects of pretreatment with the 2 main n-3 polyunsatd. fatty acids in FO, eicosapentaenoic acid (C20:5n-3; EPA) and docosahexaenoic acid, (C22:6n-3; DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA suppressed IL-6 superinduction by **DON** and impaired the **DON**-induced ERK1/2 and JNK1/2 phosphorylation. The n-6 polyunsatd. arachidonic acid (C20:4n-3) had markedly less effects on these MAPKs. Thus, the capacity of FO and its component n-3 fatty acids to suppress IL-6 expression and ERK 1/2 and JNK 1/2 activation might help explain the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:581758 CAPLUS
DOCUMENT NUMBER: 132:165241
TITLE: Fusarium mycotoxins: a review of global implications for animal health, welfare and productivity
AUTHOR(S): D'Mello, J. P. F.; Placinta, C. M.; Macdonald, A. M. C.
CORPORATE SOURCE: Department of Biotechnology, The Scottish Agricultural College, Edinburgh, UK
SOURCE: Animal Feed Science and Technology (1999), 80(3-4), 183-205
CODEN: AFSTDH; ISSN: 0377-8401
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with many refs., is given on Fusarium mycotoxicol. that covers issues such as metabolism, syndromes, interactions, residues, tolerance limits and amelioration. Trichothecenes, zearalenone (ZEN) and fumonisins are the major Fusarium mycotoxins occurring on a worldwide basis in cereal grains, animal feeds and forages. Other important Fusarium mycotoxins include moniliformin and fusaric acid. Spontaneous outbreaks of Fusarium mycotoxicoses were recorded in Europe, Asia, New Zealand and South America and chronic exposure occurs on a regular and more widespread scale. The metabolism and adverse effects of the Fusarium mycotoxins are considered in this review with particular reference to recent data on specific and proposed syndromes and to interactions among co-occurring mycotoxins. Within the **trichothecene** group, deoxynivalenol (**DON**) is associated with emesis, feed refusal and depressed feed intake in pigs, while T-2 toxin and diacetoxyscirpenol (DAS) are now clearly linked with **oral** lesions in poultry. The gut microflora of farm livestock are able to transform **DON** to a de-epoxy derivative But the ovine metabolism of ZEN gave five metabolites and relatively high levels of these forms may be excreted in the urine as glucuronides. There is now undisputed evidence that ZEN and its metabolites possess estrogenic activity in pigs, cattle and sheep, but T-2 toxin also was implicated in reproductive disorders in farm livestock. Fumonisins are pos. linked with pulmonary edema in pigs, leukoencephalomalacia in equines and with deranged sphingolipid metabolism in these animals. Fusarium mycotoxins also were provisionally implicated in ovine ill-thrift, acute mortality of poultry and in duodenitis/proximal jejunitis of horses. Several Fusarium mycotoxins may co-occur in a particular feed ingredient or in compound feeding stuffs. In general, combinations of Fusarium mycotoxins result in additive effects, but synergistic and/or potentiating interactions were observed and are of greater concern in livestock health and productivity. Synergistic effects were reported between **DON** and fusaric acid; **DON** and fumonisin B1 (FB1); and DAS and the Aspergillus-derived aflatoxins. Limited evidence of potentiation between FB1 and **DON** or T-2 toxin has also emerged recently. Additive and synergistic effects between known and unidentified mycotoxins may account for enhanced adverse effects observed on feeding Fusarium-contaminated **diets**. The potential for transmission of **DON** into eggs and of ZEN into porcine kidney and liver was demonstrated. However, lactational carry-over of FB1 appears not to occur, at least in cows and sows. Livestock health, welfare and productivity may be severely compromised by consumption of **DON**, T-2 toxin, DAS, ZEN and fumonisins and by interactions among these mycotoxins. Safety of some animal products may also be at risk. Also, in view of the limited options available for remediation, exploitation of crops resistant to Fusarium infection offers the most viable strategy for reducing mycotoxin contamination of grain and animal feed.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:690714 CAPLUS

DOCUMENT NUMBER: 130:62269

TITLE: The effects of trichothecenes on host defense against infectious diseases

AUTHOR(S): Sugita-Konishi, Yoshiko; Hara-Kudo, Yukiko; Kasuga, Fumiko; Kumagai, Susumu

CORPORATE SOURCE: Dep. Biomed. Food Res., Natl. Inst. Infectious Diseases, Toyama, Shinjuku-ku, Tokyo, 162-8640, Japan

SOURCE: Maikotokishin (Tokyo) (1998), 47, 19-23
CODEN: MAIKD3; ISSN: 0285-1466

PUBLISHER: Maikotokishin Kenkyukai

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors studied the effect of relatively low doses of 5 trichothecenes (deoxynivalenol (**DON**), diacetoxyscipenol (DAS), T-2 toxin (T-2), fusarenon-X (FX) and nivalenol (NIV)) on the host resistance against Salmonella infection using mice. Mice given daily each **trichothecene** in drinking water were infected **orally** with Salmonella enteritidis 14 days after the commencement of exposure to trichothecenes. It was found that **DON** was most effective among 5 **trichothecene** derivs. in decreasing the resistance against Salmonella infection. This effect of **DON** was associated with the reduction of serum anti-Salmonella IgM titer and delayed type hypersensitivity reaction, both of which are regarded as defense mechanisms against Salmonella infection. These results suggest that **dietary** exposure to low doses of **DON** enhances the susceptibility to **oral** infection to Salmonella through toxic effects on cellular and humoral immunity.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2005:57290 USPATFULL
TITLE: Method of treating and preventing cancer
INVENTOR(S): Kaufmann, Doug A., Rockwall, TX, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005049207	A1	20050303	
APPLICATION INFO.:	US 2003-674145	A1	20030929	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-499976P	20030903 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Michael A. O'Neil, Michael A. O'Neil, P.C., Suite 820, 5949 Sherry Lane, Dallas, TX, 75225
NUMBER OF CLAIMS: 62
EXEMPLARY CLAIM: 1
LINE COUNT: 1657
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention comprises a method of treating cancer. Specifically, the method involves administering one or more anti-fungal agents in amounts, at frequencies, and for durations which are effective in preventing and treating cancer. The method further comprises the administration of a low carbohydrate **diet** which may be used either in combination with the aforesaid anti-fungal agent or separately therefrom.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2004:133977 USPATFULL
TITLE: Novel multi-ring organic compounds for regulating gut motility and **food intake**
INVENTOR(S): Krantis, Anthony, Ontario, CANADA
Durst, Tony, Ontario, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004102514	A1	20040527	
APPLICATION INFO.:	US 2003-250986	A1	20031205	(10)
	WO 2002-CA25		20020111	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Leon R Yankwich, Yankwich & Associates, 201 Broadway,

Cambridge, MA, 02139
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Page(s)
LINE COUNT: 2424
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Multi-ring organic compounds useful in compositions and methods for regulating gut motility to modulate **food intake** and treat **obesity** and malnutrition are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 6 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2000:57940 USPATFULL
TITLE: Tolerance of **trichothecene** mycotoxins in plants and animals through the modification of the peptidyl transferase gene
INVENTOR(S): Harris, Linda, Greely, Canada
Gleddie, Steve, Ottawa, Canada
PATENT ASSIGNEE(S): Her Majesty the Queen in right of Canada, as represented by the Minister of Agriculture, Canada (non-U.S. government)
Agri-Food Canada, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6060646		20000509	
APPLICATION INFO.:	US 1997-909828		19970812	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Campell, Bruce R.
LEGAL REPRESENTATIVE: Rothwell, Figg, Ernst & Kurz, P.C.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1,9
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 1172
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Fusarium graminearum is a plant pathogen, attacking a wide range of plant species including corn (ear and stalk rot), barley, and wheat (head blight). Fusarium epidemics result in millions of dollars of loses in crop revenues. Fusarium graminearum infection in the cereals reduces both grain yield and quality. Mycotoxins are produced by many fungal Fusarium species and thus the grain becomes contaminated with these mycotoxins, such as the trichothecenes. The major **trichothecene** produced by F. graminearum is deoxynivalenol (abbreviated as **DON**, also known as vomitoxin). Trichothecenes are potent protein synthesis inhibitors and are quite toxic to humans and livestock. A yeast gene has been identified which is resistant to the **trichothecene**, trichodermin. A corresponding plant gene has been prepared, which has been used to transform plants and would be suitable to transform animals. These transformed plants have an increased resistance to Fusarium infestation. Potentially, transformed animals could have an increased tolerance to the **trichothecene** mycotoxins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 7 OF 20 USPATFULL on STN
ACCESSION NUMBER: 95:31988 USPATFULL
TITLE: **Trichothecene** conjugates
INVENTOR(S): Theodore, Louis J., 622 152nd Pl., SW., Lynnwood, WA, United States 98037
Reno, John M., 2452 Elm Dr., Brier, WA, United States 98036

Kasina, Sudhakar, 13710 115th Ave. NE., Kirkland, WA, United States 98034
Sanderson, James A., 1539 NE. 103rd Ave., Seattle, WA, United States 98125
Abrams, Paul G., 2125 First Ave., #1602, Seattle, WA, United States 98121

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5405966		19950411
APPLICATION INFO.:	US 1993-73118		19930607 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-943184, filed on 10 Sep 1992, now abandoned which is a continuation of Ser. No. US 1988-194642, filed on 16 May 1988, now patented, Pat. No. US 5157104, issued on 20 Oct 1992 which is a continuation-in-part of Ser. No. US 1985-788325, filed on 17 Oct 1985, now patented, Pat. No. US 4744981, issued on 17 May 1988

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fan, Jane T.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 1182
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugates of trichothecenes and agents that bind to a defined population of cells are disclosed. Preferred are conjugates of **trichothecene** molecules with polyclonal or monoclonal antibodies or fragments thereof that recognize antigens that are present only on tumor cells or are augmented in their expression on tumor cells as compared to normal tissues. **Trichothecene** molecules are coupled to the agent through non-covalent and covalent linkages, such as peptide bonds, disulfide bonds, thioester bonds, or thioether bonds. A method for inhibiting the growth and metabolism of antigen-positive cells is also disclosed. Derivatized **trichothecene** compounds prepared for conjugation to targeting agents are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 20 USPATFULL on STN
ACCESSION NUMBER: 92:87034 USPATFULL
TITLE: **Trichothecene** conjugates
INVENTOR(S): Sivam, Gowsala, Edmonds, WA, United States
Abrams, Paul G., Seattle, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5157104		19921020
APPLICATION INFO.:	US 1988-194642		19880516 (7)

DISCLAIMER DATE: 20050517
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1985-788325, filed on 17 Oct 1985, now patented, Pat. No. US 4744981, issued on 17 May 1988
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Cashion, Jr., Merrell C.
ASSISTANT EXAMINER: Rozycki, Andrew G.
LEGAL REPRESENTATIVE: Seed and Berry
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1,2
LINE COUNT: 547

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugates of trichothecenes and agents that bind to a defined population of cells are disclosed. Preferred are conjugates of **trichothecene** molecules with polyclonal or monoclonal antibodies or fragments thereof that recognize antigens that are present only on tumor cells or are augmented in their expression on tumor cells as compared to normal tissues. **Trichothecene** molecules are coupled to the agent through non-covalent and covalent linkages, such as peptide bonds, disulfide bonds, thioester bonds, or thioether bonds. A method for inhibiting the growth and metabolism of antigen-positive cells is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 9 OF 20 USPATFULL on STN

ACCESSION NUMBER:	90:17501 USPATFULL		
TITLE:	**Trichothecene** conjugates and methods of use		
INVENTOR(S):	Sivam, Gowsala, Edmonds, WA, United States		
PATENT ASSIGNEE(S):	Neorx Corporation, Seattle, WA, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4906452		19900306
APPLICATION INFO.:	US 1988-187113		19880428 (7)
DISCLAIMER DATE:	20050517		
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1985-788325, filed on 17 Oct 1985, now patented, Pat. No. US 4744981, issued on 17 May 1988		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Rosen, Sam		
LEGAL REPRESENTATIVE:	Leith, Debra		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	1,6		
LINE COUNT:	536		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugates of trichothecenes and agents that bind to a defined population of cells are disclosed. Preferred are conjugates of **trichothecene** molecules with polyclonal or monoclonal antibodies or fragments thereof that recognize antigens that are present only on tumor cells or are augmented in their expression on tumor cells as compared to normal tissues. **Trichothecene** molecules are coupled to the agent through non-covalent and covalent linkages, such as peptide bonds, disulfide bonds, thioester bonds, or thioether bonds. Methods for reducing intoxification in a recipient of a **trichothecene** and an agent and for producing a **trichothecene** conjugate with improved solubility are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 10 OF 20 MEDLINE on STN

ACCESSION NUMBER:	2003608631 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 14690764
TITLE:	Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil.
AUTHOR:	Moon Yuseok; Pestka James J
CORPORATE SOURCE:	Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI 48824-1224, USA.
CONTRACT NUMBER:	DK058833 (NIDDK) ES 09521 (NIEHS)

SOURCE: Journal of nutritional biochemistry, (2003 Dec) 14 (12) 717-26.
Journal code: 9010081. ISSN: 0955-2863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20031224
Last Updated on STN: 20040723
Entered Medline: 20040722

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperelevation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses **DON**-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G **diet** amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to **DON** by **oral** gavage. **DON**-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance **DON**-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E2, were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5[n-3]; EPA) and docosahexaenoic acid, (22:6[n-3]; DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by **DON**, as well as impaired **DON**-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4[n-3]) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy.

L9 ANSWER 11 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:94382 BIOSIS
DOCUMENT NUMBER: PREV200400094271
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil.
AUTHOR(S): Moon, Yuseok; Pestka, James J. [Reprint Author]
CORPORATE SOURCE: Department of Food Science and Human Nutrition, Michigan State University, East Lansing, MI, 48824-1224, USA
pestka@msu.edu
SOURCE: Journal of Nutritional Biochemistry, (December 2003) Vol. 14, No. 12, pp. 717-726. print.
CODEN: JNBIEL. ISSN: 0955-2863.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 2004

Last Updated on STN: 11 Feb 2004

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperelevation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses **DON**-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G **diet** amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to **DON** by **oral** gavage. **DON**-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance **DON**-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E2, were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5(n-3); EPA) and docosahexaenoic acid, (22:6(n-3); DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by **DON**, as well as impaired **DON**-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4(n-3)) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy.

L9 ANSWER 12 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:494316 BIOSIS
DOCUMENT NUMBER: PREV199900494316
TITLE: Fusarium mycotoxins: A review of global implications for animal health, welfare and productivity.
AUTHOR(S): D'Mello, J. P. F. [Reprint author]; Placinta, C. M.; Macdonald, A. M. C.
CORPORATE SOURCE: Department of Biotechnology, Scottish Agricultural College, West Mains Road, Edinburgh, EH9 3JG, UK
SOURCE: Animal Feed Science and Technology, (Aug. 30, 1999) Vol. 80, No. 3-4, pp. 183-205. print.
CODEN: AFSTDH. ISSN: 0377-8401.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 1999
Last Updated on STN: 16 Nov 1999

AB Trichothecenes, zearalenone (ZEN) and fumonisins are the major Fusarium mycotoxins occurring on a worldwide basis in cereal grains, animal feeds and forages. Other important Fusarium mycotoxins include moniliformin and fusaric acid. Spontaneous outbreaks of Fusarium mycotoxicoses have been recorded in Europe, Asia, New Zealand and South America and, in addition, chronic exposure occurs on a regular and more widespread scale. The metabolism and adverse effects of the Fusarium mycotoxins are considered in this review with particular reference to recent data on specific and proposed syndromes and to interactions among co-occurring mycotoxins.

Within the **trichothecene** group, deoxynivalenol (**DON**) is associated with emesis, feed refusal and depressed feed intake in pigs, while T-2 toxin and diacetoxyscirpenol (DAS) are now clearly linked with **oral** lesions in poultry. The gut microflora of farm livestock are able to transform **DON** to a de-epoxy derivative. In contrast, the ovine metabolismof ZEN results in the production of five metabolites and relatively high levels of these forms may be excreted in the urine as glucuronides. There is now undisputed evidence that ZEN and its metabolites possess estrogenic activity in pigs, cattle and sheep, but T-2 toxin has also been implicated in reproductive disorders in farm livestock. Fumonisins are positively linked with pulmonary edema in pigs, leukoencephalomalacia in equines and with deranged sphingolipid metabolism in these animals. Fusarium mycotoxins have also been provisionally implicated in ovine ill-thrift, acute mortality of poultry and in duodenitis/proximal jejunitis of horses. Several Fusarium mycotoxins may co-occur in a particular feed ingredient or in compound feedingstuffs. In general, combinations of Fusarium mycotoxins result in additive effects, but synergistic and/or potentiating interactions have been observed and are of greater concern in livestock health and productivity. Synergistic effects have beenreported between **DON** and fusaric acid; **DON** and fumonisin B1 (FB1); and DAS and the Aspergillus-derived aflatoxins. Limited evidence of potentiation between FB1 and **DON** or T-2 toxin has also emerged recently. Additive and synergistic effects between known and unidentified mycotoxins may account for enhanced adverse effects observed on feeding Fusarium-contaminated **diets**. The potential for transmission of **DON** into eggs and of ZEN into porcine kidney and liver has been demonstrated. However, lactational carry-over of FB1 appears not to occur, at least in cows and sows. It is concluded that livestock health, welfare and productivity may be severely compromised by consumption of **DON**, T-2 toxin, DAS, ZEN and fumonisins and by interactions among these mycotoxins. Safety of some animal products may also be at risk. Furthermore, in view of the limited options available for remediation, it is concluded that exploitation of crops resistant to Fusarium infection offers the most viable strategy for reducing mycotoxin contamination of grain and animal feed.

L9 ANSWER 13 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004006762 EMBASE
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil.
AUTHOR: Moon Y.; Pestka J.J.
CORPORATE SOURCE: J.J. Pestka, Dept. of Food Sci. and Hum. Nutr., Michigan State University, East Lansing, MI 48824-1224, United States. pestka@msu.edu
SOURCE: Journal of Nutritional Biochemistry, (2003) Vol. 14, No. 12, pp. 717-726.
Refs: 77
ISSN: 0955-2863 CODEN: JNBIEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040116
Last Updated on STN: 20040116

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperelevation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses

DON-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G **diet** amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to **DON** by **oral** gavage. **DON**-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases 1 and 2 (ERK1/2) and c-Jun N-terminal kinases 1 and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance **DON**-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E(2,) were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5[n-3]; EPA) and docosahexaenoic acid, (22:6[n-3]; DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by **DON**, as well as impaired **DON**-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4[n-3]) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy.

L9 ANSWER 14 OF 20 SCISEARCH

ACCESSION NUMBER: 2005:243714 SCISEARCH
THE GENUINE ARTICLE: 899NW
TITLE: Truncated deoxynivalenol-induced splenic immediate early gene response in mice consuming (n-3) polyunsaturated fatty acids
AUTHOR: Kinser S; Li M X; Jia Q S; Pestka J J (Reprint)
CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Ctr Integrat Toxicol, E Lansing, MI 48824 USA; Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NUTRITIONAL BIOCHEMISTRY, (FEB 2005) Vol. 16, No. 2, pp. 88-95.
Publisher: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA.
ISSN: 0955-2863.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Expression profiling has previously revealed that acute exposure to the common foodborne mycotoxin deoxynivalenol (**DON**) induces a large number of immediate early genes in murine lymphoid tissues that potentially affect immune function. The purpose of this study was to test the hypothesis that consumption of (n-3) polyunsaturated fatty acids (PUFAs) found in fish oil interferes with **DON**-induced immediate early gene expression. Mice were fed AIN-93G **diet** containing 1% corn oil (CO) plus 6% oleic acid (control) or a **diet** containing 1% CO, 2% fish oil enriched in the (n-3)-PUFAs docosahexaenoic and eicosapentaenoic acid and 4% oleic acid. After 12 weeks, the mice were gavaged **orally** with 25 mg/kg **DON** and the kinetics of immediate early gene expression in spleen monitored over 8 h by real-time

polymerase chain reaction (PCR). Deoxynivalenol was found to readily induce expression of cytokines (IL-1alpha, IL-1beta, and IL-6 and IL-11), chemokines (MCP-1, MCP-3, CINC-1 and MIP-2), components of the activator protein-1 (AP-1) transcription factor complex (c-Fos, Fra-2, c-Jun and JunB), as well as two hydrolases (MKP1, CnAbeta). Expression of these genes was transient, peaking within 2-4 h and declining thereafter, with the single exception being IL-11 that was elevated at 8 h. (n-3)-PUFA consumption significantly suppressed **DON**-induced expression of IL-1alpha, IL-6, IL-11, MCP-1, MCP-3, MIP-2 and Fra-2 at 8 h. In contrast, mice fed (n-3),-PUFA exhibited significant increases in MKP1 and CnAbeta expression. Taken together, these data suggest that **dietary** supplementation with (n-3)-PUFAs prematurely truncated cytokine. chemokine and transcription factor expression responses to **DON** that may impact its previously described capacity to disrupt immune function including immunoglobulin A (IgA) production. Since expression of many of these genes has been linked to mitogen-activated protein kinase (MAPK) activation, enhanced expression of MKP1, a negative MAPK regulator in (n-3)-PUFA-fed mice might contribute to this suppression. (C) 2005 Published by Elsevier Inc.

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ACCESSION NUMBER: 2005:42425 SCISEARCH
THE GENUINE ARTICLE: 879LY
TITLE: Docosahexaenoic acid attenuates mycotoxin-induced immunoglobulin a nephropathy, interleukin-6 transcription, and mitogen-activated protein kinase phosphorylation in mice
AUTHOR: Jia Q S; Zhou H R; Bennink M; Pestka J J (Reprint)
CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48823 USA (Reprint); Michigan State Univ, Ctr Integrat Toxicol, E Lansing, MI 48823 USA; Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48823 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NUTRITION, (DEC 2004) Vol. 134, No. 12, pp. 3343-3349.
Publisher: AMER INST NUTRITION, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0022-3166.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 66

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The purpose of this investigation was to evaluate the dose-dependent effects of docosahexaenoic acid (DHA) on deoxynivalenol (**DON**)-induced IgA nephropathy in mice and their relation to proinflammatory gene expression and mitogen-activated protein kinase (MAPK) activation. Consumption of a modified AIN-93G **diet** containing 1, 5, and 30 g/kg DHA resulted in dose-dependent increases of DHA in liver phospholipids with concomitant decreases in arachidonic acid compared with control **diets**. DHA dose dependently inhibited increases in serum IgA and IgA immune complexes (IC) as well as IgA deposition in the kidney in **DON**-fed mice; the 30 g/kg DHA **diet** had the earliest detectable effects and maximal efficacy. Both splenic interleukin-6 (IL-6) mRNA and heterogeneous nuclear RNA (hnRNA), an indicator of IL-6 transcription, were significantly reduced in **DON**-fed mice that consumed 5 and 30 g/kg DHA; a similar reduction was observed for cyclooxygenase (COX-2) mRNA. In a subsequent study, acute **DON** exposure (25 mg/kg body weight) induced splenic IL-6 mRNA and hnRNA as well as COX-2 mRNA in mice fed the control **diet**, whereas induction of both RNA species was significantly inhibited in mice fed 30 g/kg DHA. These latter inhibitory effects corresponded to a reduction in **DON**-induced phosphorylation of p38, extracellular-signal related

kinase 1/2, and c-Jun N-terminal kinase 1/2 MAPKs in the spleen. Taken together, the results indicate that DHA dose-dependently inhibited **DON**-induced IgA dysregulation and nephropathy, and that impairment of MAPK activation and expression of COX-2 and IL-6 are potential critical upstream mechanisms.

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ACCESSION NUMBER: 2004:557459 SCISEARCH
THE GENUINE ARTICLE: 827IN
TITLE: Docosahexaenoic acid and eicosapentaenoic acid, but not alpha-linolenic acid, suppress deoxynivalenol-induced experimental IgA nephropathy in mice
AUTHOR: Jia Q S; Shi Y H; Bennink M B; Pestka J J (Reprint)
CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA; Michigan State Univ, Ctr Integrat Toxicol, E Lansing, MI 48824 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NUTRITION, (JUN 2004) Vol. 134, No. 6, pp. 1353-1361.
Publisher: AMER INST NUTRITION, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0022-3166.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 67

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Diets** enriched in the (n-3) PUFAs, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and their precursor a-linolenic acid (ALA), were evaluated for efficacy in ameliorating the development of IgA nephropathy (IgAN) induced in mice by the mycotoxin deoxynivalenol (**DON**). The effects of **DON** were compared in mice that were fed for 18 wk with AIN-93G **diets** containing 1) 10 g/kg corn oil plus 60 g/kg oleic acid (control); 2) 10 g/kg corn oil plus 35 g/kg oleic acid and 25 g/kg DHA-enriched fish oil (DHA); 3) 10 g/kg corn oil plus 33 g/kg oleic acid and 27 g/kg EPA-enriched fish oil (EPA); and 4) 10 g/kg corn oil plus 37 g/kg oleic acid and 23 g/kg DHA + EPA (1:1) enriched fish oil (DHA + EPA). The DHA, EPA and DHA + EPA **diets** attenuated induction by **dietary DON** (10 mg/kg) of serum IgA and IgA immune complexes, kidney mesangial IgA deposition, and ex vivo IgA secretion by spleen cells. Consumption of the DHA + EPA **diet** for 8 wk significantly abrogated the **DON**-induced gene expression of interleukin (IL)-6, a requisite cytokine for **DON**-induced IgA nephropathy, in spleen and Peyer's patches. Finally, incorporation of ALA-containing flaxseed oil up to 60 g/kg in the AIN-93G **diet** did not affect **DON**-induced IgA dysregulation in mice. Taken together, both DHA and EPA, but not ALA, ameliorated the early stages of IgAN, and these effects might be related to a reduced capacity for IL-6 production.

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ACCESSION NUMBER: 2004:39516 SCISEARCH
THE GENUINE ARTICLE: 757ML
TITLE: Deoxynivalenol-induced mitogen-activated protein kinase phosphorylation and IL-6 expression in mice suppressed by fish oil
AUTHOR: Moon Y; Pestka J J (Reprint)
CORPORATE SOURCE: Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Inst Environm Toxicol, E Lansing, MI 48824 USA; Michigan State Univ, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA

COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NUTRITIONAL BIOCHEMISTRY, (DEC 2003) Vol. 14, No. 12, pp. 717-726.
Publisher: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA.
ISSN: 0955-2863.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 77

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The **trichothecene** mycotoxin deoxynivalenol (**DON**) induces IgA hyperelevation and mesangial IgA deposition in mice that mimics the early stages of human IgA nephropathy (IgAN). Among potential mediators of this disease, interleukin-6 (IL-6) is likely to play a particularly critical role in IgA elevation and disease exacerbation. Based on previous findings that **dietary** fish oil (FO) suppresses **DON**-induced IgAN, we hypothesized that FO inhibits the induction of IL-6 expression by this mycotoxin in vivo and in vitro. Mice were fed modified AIN 93G **diet** amended with 7% corn oil (CO) or with 1% corn oil plus 6% menhaden fish oil (FO) for up to 8 weeks and then exposed acutely to **DON** by **oral** gavage. **DON**-induced plasma IL-6 and splenic mRNA elevation in FO-fed mice were significantly suppressed after 8 weeks when compared to the CO-fed group. The effects of FO on phosphorylation of mitogen-activated protein kinases (MAPKs), critical upstream transducers of IL-6 up-regulation, were also assessed. **DON**-induced phosphorylation of extracellular signal regulated protein kinases I and 2 (ERK1/2) and c-Jun N-terminal kinases I and 2 (JNK1/2) was significantly suppressed in spleens of mice fed with FO, whereas p38 was not. Splenic COX-2 mRNA expression, which has been previously shown to enhance **DON**-induced IL-6, was also significantly decreased by FO, whereas plasma levels of the COX-2 metabolite, prostaglandin E-2, were not affected. To confirm in vivo findings, the effects of pretreatment with the two primary n-3 PUFAs in FO, eicosapentaenoic acid (20:5[n-3]; EPA) and docosahexaenoic acid, (22:6[n-3]; DHA), on **DON**-induced IL-6 expression were assessed in LPS-treated RAW 264.7 macrophage cells. Consistent with the in vivo findings, both EPA and DHA significantly suppressed IL-6 superinduction by **DON**, as well as impaired **DON**-induced ERK1/2 and JNK1/2 phosphorylation. In contrast, the n-6 PUFA arachidonic acid (20:4[n-3]) had markedly less effects on these MAPKs. Taken together, the capacity of FO and its component n-3 PUFAs to suppress IL-6 expression as well as ERK 1/2 and JNK 1/2 activation might explain, in part, the reported suppressive effects of these lipids on **DON**-induced IgA nephropathy. (C) 2003 Elsevier Inc. All rights reserved.

ACCESSION NUMBER: 2003:365843 SCISEARCH
THE GENUINE ARTICLE: 668RX
TITLE: Deoxynivalenol-induced IgA production and IgA nephropathy-aberrant mucosal immune response with systemic repercussions
AUTHOR: Pestka J J (Reprint)
CORPORATE SOURCE: Michigan State Univ, Inst Environm Toxicol, Dept Food Sci & Human Nutr, Dept Microbiol & Mol Genet, 234 GM Trout Food Sci & Human Nutr Bldg, E Lansing, MI 48824 USA (Reprint); Michigan State Univ, Inst Environm Toxicol, Dept Food Sci & Human Nutr, Dept Microbiol & Mol Genet, E Lansing, MI 48824 USA
COUNTRY OF AUTHOR: USA
SOURCE: TOXICOLOGY LETTERS, (11 APR 2003) Vol. 140, Sp. iss. SI, pp. 287-295.
Publisher: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS

MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND.
ISSN: 0378-4274.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 63

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Dietary** exposure to the common foodborne mycotoxin deoxynivalenol (**DON**) selectively upregulates serum immunoglobulin A (IgA) in the mouse, most of which is polymeric, thus suggesting that the mucosal immune system is a primary target. When ingested, **DON** has no adjuvant or antigen properties but, rather, induces polyclonal IgA synthesis and serum elevation in an isotype-specific fashion. Resultant hyperelevated IgA is polyspecific, autoreactive and is likely to be involved in immune complex formation as well as kidney mesangial deposition. These latter effects mimic IgA nephropathy, the most common human glomerulonephritis. At the cellular level, **DON** upregulates production of T helper cytokines and enhances T cell help for IgA secretion. Analogous effects are observed in the macrophage with IL-6 being of particular importance based on ex vivo reconstitution and antibody ablation studies as well as experiments with IL-6 deficient mice, Upregulation of cytokines by **DON** involves both increased transcriptional activation and mRNA stability which are mediated by activation of mitogen-activated protein kinases. Interestingly, **dietary** omega-3 fatty acids can downregulate these processes and ameliorate **DON**-induced IgA nephropathy. From the perspective of gut mucosal immunotoxicology, these studies demonstrate that the capacity of a chemical to affect mucosal immune response can have systemic repercussions and, further, that these effects can be modulated by an appropriate nutritional intervention. (C) 2003 Elsevier Science Ireland Ltd. All rights reserved.

L9 ANSWER 19 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:729862 SCISEARCH
THE GENUINE ARTICLE: 237TB
TITLE: Fusarium mycotoxins: a review of global implications for animal health, welfare and productivity
AUTHOR: DMello J P F (Reprint); Placinta C M; Macdonald A M C
CORPORATE SOURCE: SCOTTISH AGR COLL, DEPT BIOTECHNOL, W MAINS RD, EDINBURGH EH9 3JG, MIDLOTHIAN, SCOTLAND (Reprint)
COUNTRY OF AUTHOR: SCOTLAND
SOURCE: ANIMAL FEED SCIENCE AND TECHNOLOGY, (30 AUG 1999) Vol. 80, No. 3-4, pp. 183-205.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0377-8401.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: English
REFERENCE COUNT: 93

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Trichothecenes, zearalenone (ZEN) and fumonisins are the major Fusarium mycotoxins occurring on a worldwide basis in cereal grains, animal feeds and forages. Other important Fusarium mycotoxins include moniliformin and fusaric acid. Spontaneous outbreaks of Fusarium mycotoxicoses have been recorded in Europe, Asia, New Zealand and South America and, in addition, chronic exposure occurs on a regular and more widespread scale. The metabolism and adverse effects of the Fusarium mycotoxins are considered in this review with particular reference to recent data on specific and proposed syndromes and to interactions among co-occurring mycotoxins. Within the **trichothecene** group, deoxynivalenol (**DON**) is associated with emesis, feed refusal and depressed feed intake in pigs,

while T-2 toxin and diacetoxyscirpenol (DAS) are now clearly linked with **oral** lesions in poultry. The gut microflora of farm livestock are able to transform **DON** to a de-epoxy derivative. In contrast, the ovine metabolism of ZEN results in the production of five metabolites and relatively high levels of these forms may be excreted in the urine as glucuronides. There is now undisputed evidence that ZEN and its metabolites possess estrogenic activity in pigs, cattle and sheep, but T-2 toxin has also been implicated in reproductive disorders in farm livestock. Fumonisins are positively linked with pulmonary edema in pigs, leukoencephalomalacia in equines and with deranged sphingolipid metabolism in these animals. Fusarium mycotoxins have also been provisionally implicated in ovine ill-thrift, acute mortality of poultry and in duodenitis/proximal jejunitis of horses. Several Fusarium mycotoxins may co-occur in a particular feed ingredient or in compound feedingstuffs. In general, combinations of Fusarium mycotoxins result in additive effects, but synergistic and/or potentiating interactions have been observed and are of greater concern in livestock health and productivity. Synergistic effects have been reported between **DON** and fusaric acid; **DON** and fumonisin B-1 (FB1); and DAS and the Aspergillus-derived aflatoxins. Limited evidence of potentiation between FB1 and **DON** or T-2 toxin has also emerged recently Additive and synergistic effects between known and unidentified mycotoxins may account for enhanced adverse effects observed on feeding Fusarium-contaminated **diets**. The potential for transmission of **DON** into eggs and of ZEN into porcine kidney and liver has been demonstrated. However, lactational carry-over of FB1 appears not to occur, at least in cows and sows. It is concluded that livestock health, welfare and productivity may be severely compromised by consumption of **DON**, T-2 toxin, DAS, ZEN and fumonisins and by interactions among these mycotoxins. Safety of some animal products may also be at risk. Furthermore, in view of the limited options available for remediation, it is concluded that exploitation of crops resistant to Fusarium infection offers the most viable strategy for reducing mycotoxin contamination of grain and animal feed.

L9 ANSWER 20 OF 20 SCISEARCH

ACCESSION NUMBER: 97:741663 SCISEARCH
THE GENUINE ARTICLE: XZ071
TITLE: Transformation of nivalenol by gastrointestinal microbes
AUTHOR: Hedman R (Reprint); Pettersson H
CORPORATE SOURCE: SWEDISH UNIV AGR SCI, DEPT ANIM NUTR & MANAGEMENT, POB 7024, S-75007 UPPSALA, SWEDEN (Reprint)
COUNTRY OF AUTHOR: SWEDEN
SOURCE: ARCHIVES OF ANIMAL NUTRITION-ARCHIV FUR TIERERNAHRUNG, (15 AUG 1997) Vol. 50, No. 4, pp. 321-329.
Publisher: HARWOOD ACAD PUBL GMBH, C/O STBS LTD, PO BOX 90, READING, BERKS, ENGLAND RG1 8JL.
ISSN: 0003-942X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: AGRI
LANGUAGE: English
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND ALL FORMATS

AB The capacity of the gastrointestinal microflora of pig, cow, and chicken to metabolize nivalenol (NIV) and deoxynivalenol (**DON**) was studied both in vivo and in vitro. Before feeding NIV to pigs, no metabolites of NIV or **DON** were formed in anaerobic incubates of the toxins with the pigs feces. However. after one week on a **diet** containing 2.5 or 5 ppm NN, nearly all excreted NIV in feces had been de-epoxidated in five of six pigs. After three weeks on the NIV **diet** also the sixth pig had acquired this ability. Deoxynivalenol was also de-epoxidated when incubated in vitro with the microorganisms

that formed de-epoxy-NIV in vivo. Anaerobic incubation of NIV and DON with cow rumen fluid produced de-epoxides of both toxins in a high proportion. No de-epoxide of NIV, but another unidentified metabolite was found in feces from chicken fed 2.5 or 5 ppm NIV for three weeks.